Dependence of implantation angle of the transverse, intrafascicular electrode (TIME) on selective activation of pig forelimb muscles

Kundu, Aritra; Jensen, Winnie; Kurstjens, Mathijs; Stieglitz, T.; Boretius, T.; Yoshida, Ken

Published in:
Proceedings of the 10th Vienna International Workshop on Functional Electrical Stimulation and 15th IFESS Annual Conference, 8-12 September, 2010, Vienna, Austria

Publication date:
2010

Document Version
Publisher's PDF, also known as Version of record

Dependence of implantation angle of the transverse, intrafascicular electrode (TIME) on selective activation of pig forelimb muscles

Kundu A[1], Jensen W[1], Kurstjens M[1], Stieglitz T[3], Boretius T[3], Yoshida K[1,2]

[1] Center for Sensor-Motor Interaction, Dept. Health Science and Technology, Aalborg University, Denmark

[2] Biomedical Engineering Dept., Indiana University-Purdue University Indianapolis, Indianapolis, USA

[3] Laboratory for Biomedical Microtechnology, Albert-Ludwigs University, Freiburg, Germany

Abstract

The aim of the present study is to investigate the stimulation selectivity of the transverse intrafascicular multichannel electrode (TIME). The TIME is a multichannel neural prosthetic interface being developed to deliver relatively high stimulation selectivity for use in applications, such as the control of multiple-degree prosthetic devices or for eliciting sensory feedback. The electrodes were implanted in the median nerve in the upper left limb of one landrace pig at four different implantation angles (45°, 90°, 135° and 180°) with respect to the cross section of the nerve. Monopolar, 100µs long, rectangular pulses (pulse amplitude 40- 800 µA, steps of 40µA) were sequentially delivered to each of the 12 contact sites on the electrode structure to evoke muscle activation in the upper limb. The recruitment of seven muscles in upper limb was quantified as a function of stimulation. The preliminary results indicated that the selectivity of muscle activation and recruitment was dependent on the implantation angle.

Keywords: *neural interface, selective activation, intrafascicular, phantom limb pain*

Introduction

Amputation of a limb involves truncation of all afferent and efferent nerves that innervated the amputated limb. Consequent retrograde changes may impact both the peripheral nervous system and the central nervous system [1]. These changes often result in a sensation that the missing body part is still present (i.e. phantom limb awareness) and kinaesthetically perceived (i.e. phantom limb sensation). In 50-80% of all amputees, phantom limb pain (PLP) develops [2]. Today, it is not completely understood why the pain occurs, and there are no fully effective treatment.

Several studies have demonstrated that by providing appropriate sensory feedback signals to the amputee subject can assist to alleviate PLP. For example, the intensive use of myoelectric prosthesis [3], or daily training sessions involving discrimination between different surface electrical stimuli [4] applied to the stump experienced significant reduction of PLP. Intrafascicular, electrical stimulation of severed nerves proved to be capable of eliciting tactile or proprioceptive sensations by implanted LIFE electrodes in human subjects [5]. Rossini et al. also demonstrated that training for control of a robotic hand (with a limited amount of sensory feedback) significantly reduced PLP in a human amputee volunteer implanted with four LIFE electrodes [6]. The reduction in PLP lasted several weeks after the LIFE electrodes were removed and changes in sensorimotor cortex topography were shown [6].

The present work is part of an ongoing EU project 'TIME', where we hypothesize that given selective activation a sufficient number of nerve fibres, a neural interface may be able to artificially evoke sensations and eventually allieve PLP. A new generation of transverse, intrafascicular electrodes (TIME) has been developed for this purpose (see [7] for a review of development and use of the intrafascicular electrodes). The main objective of the present study was to investigate the degree of stimulation selectivity of the TIME electrodes in an animal model with nerve size similar to humans. We further investigated the morphological structure of the porcine median nerve to determine the number of fascicles in/around the implant site.

Material and Methods

Animal preparation

All experimental procedures were approved by the animal experiment inspectorate under the Danish Ministry of Justice. 7 female, Yorkshire landrace pig (<50 kg) were included in the present work. These preliminary results are from analysis of one animal (selectivity) and 6 animals (histology). The animals were placed under general anaesthesia (ventilated at 15 breaths/min, 50-50% air/oxygen, 1-1.2 % Isoflurane), received 0.9% saline to prevent dehydration and pancuronium bromide/fentanyl (Esmeron® 10mg/ml and "Hameln" 50 μg/ml) as analgesia. The animals were placed in a supine position, and access to the median nerve in the upper limb was created through the axilla. Heart rate and oxygen saturation were monitored throughout the experiment.

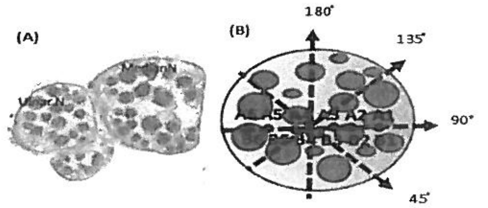

Fig 1. A) H&E stain of the median and ulnar nerves approx. 2-3 cm above the elbow joint, where the electrodes were implanted. B) Schematic drawing of electrode implantation angles of the TIME electrodes in the median nerve.

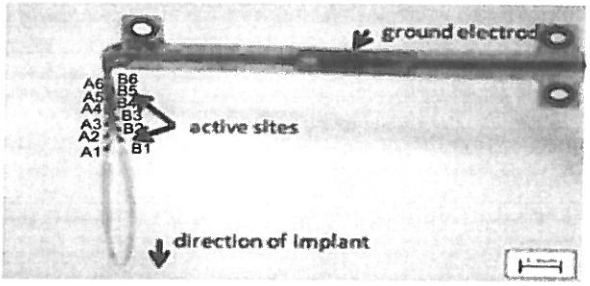

Fig 2. Transverse-intrafascicular, multi-channel electrode (TIME) with 12 active sites to be placed inside the median nerve. The broader, horizontal part of the polyimide substrate serves as insertion stop and stays outside the nerve.

The transverse, intrafascicular electrodes (TIME) were implanted in the median nerve approximately 2-3 cm above the elbow joint at implantation angles of 45°, 90°, 135° and 180° (see Fig. 1b). The TIME electrodes were manufactured at IMTEK (see Fig 2.; see [8] for detailed description). The electrode has 12 equidistant active sites with a pitch of 440 μm, with 6 contacts placed on either side of the polymide loop structure. They are referred as A1, A2, A3, A4, A5, A6 and B1, B2, B3, B4, B5, B6.

To evaluate the selective activation of individual fascicles in the median nerve, we recorded EMG responses from seven forearm muscles using bipolar patch electrodes placed at three extensor muscles (biceps brachii [M1], extensor carpi radialis [M2], extensor carpi ulnaris [M7]), three flexor muscles (flexor carpi radialis [M3], flexor digitalis superficialis [M4], flexor carpi ulnaris [M5]) and the muscle interosseus medius [M6]. We applied cathodic monopolar, rectangular constant-current pulses between the individual contacts and an external ground placed within the animal using a Multichannel Systems STG2008 stimulator. Stimuli were 100μs with amplitudes 40μA to 800μA, and presented at 2Hz. 5 pulses were repeated at each current level.

At the end of the experiment, the animal was euthanized with an overdose of sodium pentobarbital. To evaluate the morphology of the pig nerve, a nerve section were harvested immediately after euthanasia at the level of the implant and prepared for histological analysis. The specimens were placed on a metal plate, fixated with tissue glue (CryoJane) to maintain orientation of the specimen during freezing in liquid nitrogen. 5 μm frozen transverse sections of the nerve were taken and subsequently stained using H&E (see Fig. 1A).

Data analysis

Muscle activation was quatified by measuring the amplitude of the EMG amplitude. EMG signals were band-pass filtered (100 Hz - 2 kHz) and its RMS value was calculated in the period 2 – 12 ms time interval after stimulation. These values were normalized to the maximum RMS for each muscle (including data from stimulating contacts at all four implant directions) to generate recruitment curves (Fig. 3). Stimulation selectivity was then evaluated for each contact at the maximum current 800 μ A (Fig. 4), where we expect the worst-case selectivity performance.

To evaluate the morphological structure of the median nerve, the number of fascicles and fascicle diameter/area were determined at three levels of the nerve; ~3-4 cm above, at, and ~3-4cm below the level of the implant site. Digital photomicrographs were taken and analyzed using Axio Vision (Axio Vs40 v. 4.6.30, Carl Zeiss Imaging solutions GmbH, Germany).

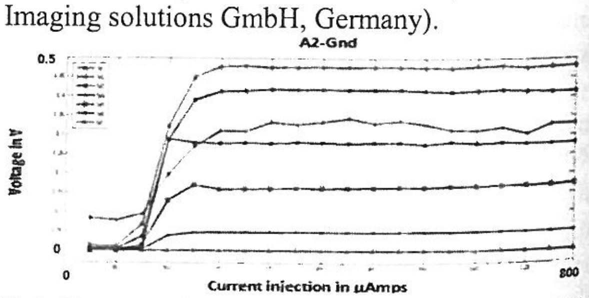

Fig 3. The generated muscle recuitment curves. X-axis represents the 20 simulation levels (40 μA to 800 μA), and the y-axis reflects the corresponding EMG activity for each of the 7 muscles.

Table 1. Results of histological evaluation from 6 nerves (left and right forelimb). All numbers are given as mean ± std. (*) indicates that 4 nerve speciments were included in the analysis

	Proximal to implant site	At implant site	Distal to implant site
Fascicle diameter [mm]	0.27 ± 0.083	0.23 ± 0.086	0.24 ± 0.093
Fascicle count	29 ± 5	36 ± 4	33 ± 8
Whole nerve diameter [mm]	No data	2.9 ± 0.4mm (*)	2.2 ± 0.6mm (*)

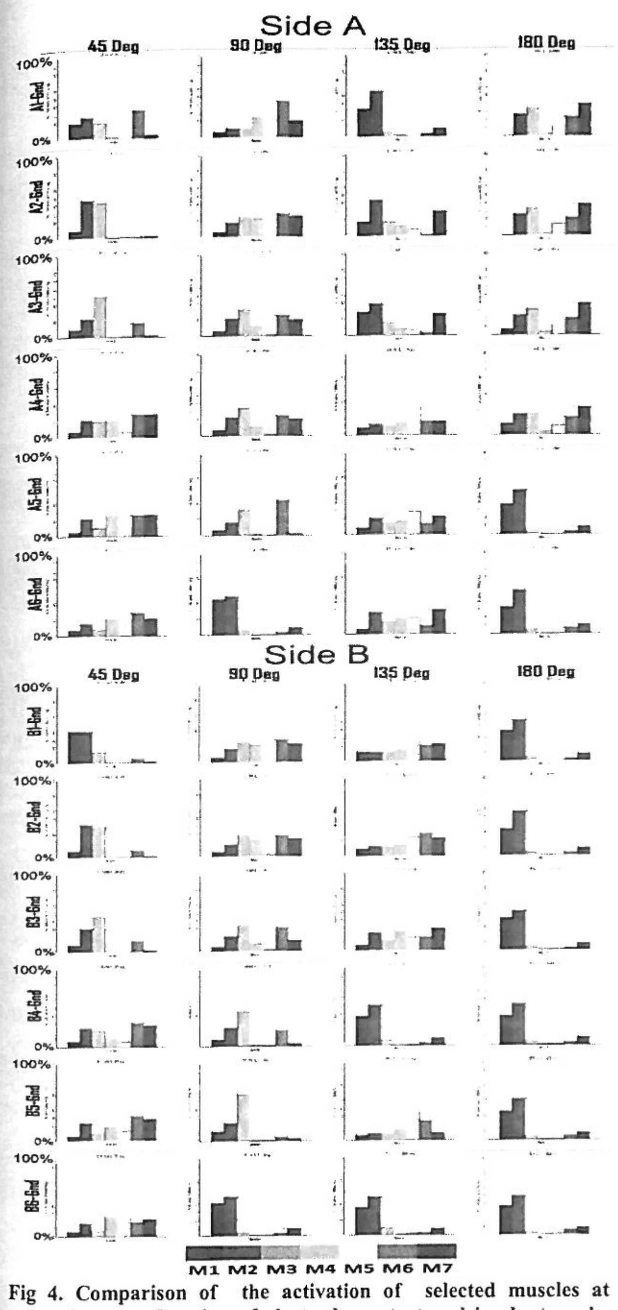

Fig 4. Comparison of the activation of selected muscles at saturation as a function of electrode contact and implant angle. Upper panel: results from stimulating 6 contacts on the side A of the electrode. Lower panel: results from stimulating the six contacts on side B .

Results

The cursory selectivity analysis (Fig. 4) indicate that there was strong possibility of activating extensor muscles (M1, M2 and M 7) when implantation is made at 180°. On the other hand, mostly the flexor muscles (M3, M4 and M5) and muscle interosseus medius (M6) were activated when the electrode was implanted at 90°. Implantation at 45° and 135° activated all seven muscles in the majority of the cases. Different orientation angles resulted in different activation characteristics.

The histological evaluation from 6 pig forelimb nerves (both left and right arm) are shown in Table 1. The median nerve contained the highest number of fascicles at the implant sited just above the elbow joint. The fascicle diameters were similar at all three levels.

Discussion and conclusions

Our objective was to investigate the stimulation selectivity of the TIME electrode within an animal model with nerve size similar to humans. These preliminary results show the importance of implantation angle on the selectivity and reachability of muscle activation. This parameter may be an important factor for optimization, where there is a trade off of reachability with selectivity. The morphological analysis revealed up to 40 fascicles at the level of implantation. Although further investigation is needed to optomize how many of these fascicles can be reached versus the number of electrode structures and contacts used, the transversely implant intrafascicular electrode may be an important step towards reaching this compromise.

Acknowledgements

This work was funded by the EU TIME project (CP-FP-INFSO 224012/TIME). Authors would like to thank O. Sørensen, T. Madsen, J. Sørensen and B. Jensen (Dept. Pathology, Aarhus University Hospital-Aalborg) for assistance in the animal experiments and preparation of nerves for histological evaluation.

Author's Address

Kundu A, Center for Sensor-Motor Interaction, Department of Health Science and Technology, Aalborg University, Fredrik Bajersvej 7D-3, 9220 Aalborg, Denmark, akundu@hst.aau.dk

References

[1] X. Navarro, M. Vivó and A. Valero-Cabré, "Neural plasticity after peripheral nerve injury and regeneration," Prog.Neurobiol., vol. 82, pp. 163-201, 2007.

[2] P.L. Ephraim, S.T. Wegener, E.J. MacKenzie, T.R. Dillingham and L.E. Pezzin, "Phantom pain, residual limb pain, and back pain in amputees: results of a national survey," Arch.Phys.Med.Rehabil., vol. 86, pp. 1910-1919, 2005.

[3] M. Lotze, W. Grodd, N. Birbaumer, M. Erb, E. Huse and H. Flor, "Does use of myoelectric prosthesis reduce cortical reorganization and phantom limb pain?" Nat.Neurosci., vol. 2, pp. 501-502, 1999.

[4] H. Flor, C. Dencke, M. Schaefer and S.M. Grusser, "Effect of sensory discrimination traning on cortical reorganization and phantom limb pain," Lancet, vol. 357, pp. 1763-1764, 2001.

[5] G.S. Dhillon and K. Horch, "Direc neural sensory feedback and control of prosthetic arm," IEEE Trans Neural Syst Rehabil Eng, vol. 13, pp. 468-472, 2005.

[6] P.M. Rossini, "Double nerve intraneural interface implant on a human amputee for robotic hand control," Accepted for Publication in Clinical Neurophysiology, 2010.

[7] K. Yoshida, D. Farina, M. Akay and W. Jensen, "Multichannel Intraneural and Intramuscular Techniques for Multiunit Recording and Use in Active Prostheses," Proc IEEE, vol. 98, pp. 432-449, 2010.

[8] T. Boretius, J. Badia, A. Pascual-Font, D. Andreu, C. Azevedo-Coste, J. Divoux, T. Stieglitz, X. Navarro and K. Yoshida, "Trans-verse Intrafascicular Multichannel Electrode (TIME) an Interface to Peripheral Nerves: Preliminary In-vivo Results in Rats," Proceedings of the 14th IFESS Conference, Seoul, South Korea, pp. 37-39, 2009.

Proceedings

of the

10^{th} Vienna International Workshop on Functional Electrical Stimulation

and

15^{th} IFESS Annual Conference, 2010

guest

Neuromodulation 2010: The way ahead

(Chair: Prof. Francois Alesch)

Vienna, Austria
September 8^{th}-12^{th}, 2010

Edited by

Thomas Mandl
Johannes Martinek
Manfred Bijak
Hermann Lanmüller
Winfried Mayr
Melitta Pichler

Published by

Center for Medical Physics and Biomedical Engineering
Medical University of Vienna, Vienna Medical School
AKH 4L
Waehringer Guertel 18-20
A-1090 Vienna
Austria

Tel.: +43-1-40400-1984
Fax: +43-1-40400-3988

http://www.fesworkshop.org
ISBN 3-900928-09-5